

PATENT COOPERATION TREATY

REC'D 29 SEP 2005

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From the
INTERNATIONAL SEARCHING AUTHORITY

To:

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2004/005438

International filing date (day/month/year)
20.12.2004

Priority date (day/month/year)
24.12.2003

International Patent Classification (IPC) or both national classification and IPC
C07K14/775, A61K38/10, A61P31/12

Applicant
THE UNIVERSITY OF MANCHESTER

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/005438

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☒ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☒ in written format
☒ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☒ furnished subsequently to this Authority for the purposes of search.
3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☐ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:
see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/005438

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 11 and 12 entirely and 10 and 17 in as far as industrial applicability is concerned

because:

- ☒ the said international application, or the said claims Nos. 10 and 17, in as far as industrial applicability is concerned relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 11,12 are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☒ the claims, or said claims Nos. 11,12 are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 11,12
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form

- ☐ has not been furnished
- ☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/005438

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	5,7,14-17
	No: Claims	1-4,6,8-10,13
Inventive step (IS)	Yes: Claims	5,7,16,17
	No: Claims	1-4,6,8-10,13-15
Industrial applicability (IA)	Yes: Claims	1-9,13-16
	No: Claims	10,17

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

The following documents are referred to in this written opinion:

- D1: WO 99/24054 A (INNOGENETICS N.V; MAERTENS, GEERT; DEPLA, ERIK) 20 May 1999 (1999-05-20)
- D2: RUGGERI Z M ET AL: "INHIBITION OF PLATELET FUNCTION WITH SYNTHETIC PEPTIDES DESIGNED TO BE HIGH-AFFINITY ANTAGONISTS OF FIBRINOGEN BINDING TO PLATELETS" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 83, no. 15, 1 August 1986 (1986-08-01), pages 5708-5712, XP000611247 ISSN: 0027-8424
- D3: CHILLEMI F ET AL: "SYNTHESIS AND CYTOTOXIC ACTIVITY OF PEPTIDES CONTAINING BASIC AMINO ACIDS RESIDUES" ANTICANCER RESEARCH, HELENIC ANTICANCER INSTITUTE, ATHENS,, GR, vol. 16, no. 2, 1996, pages 715-716, XP009034296 ISSN: 0250-7005
- D4: MOHRI H ET AL: "SYNTHETIC PEPTIDES INHIBIT THE INTERACTION OF VON WILLEBRAND FACTOR-PLATELET MEMBRANE GLYCOPROTEINS" PEPTIDES, ELSEVIER, AMSTERDAM, US, vol. 14, no. 2, 1993, pages 125-129, XP000651834 ISSN: 0196-9781
- D5: WO 91/09614 A (SCRIPPS CLINIC AND RESEARCH FOUNDATION) 11 July 1991 (1991-07-11)

Re: II

The priority document was made available to the International Searching Authority (ISA) by the International Bureau at the time of the search. The application as filed comprises some extra examples and figures, and the SEQ.ID's 34-47 were also absent from the invoked priority. This has no bearing on the interpretation of the claims in the light of the prior art revealed at present.

Re: III

For the assessment of the present claims 10 and 17 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for

example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re: V

It is not clear where in the apolipoprotein B the HSPG receptor binding region might be located. It is furthermore not clear to which entity the respective terms derivative, analogue, and truncation relate, nor how one would recognize a truncation of a tandem repeat. The scope of claim 1 therefore is not clear either, and it is impossible to even begin a novelty assessment thereof in a meaningful manner. Apolipoprotein B itself is considered prejudicial for the novelty of claim 1.

Although the boundaries of cluster B of the LDL receptor binding domain have been clearly defined in D8, cited in the application, the claims nor the description provide this information. The claims should be clear by themselves, without relying on the description for clarity. Claim 2 cannot be regarded as clear in the sense of Art.6 PCT. In fact, cluster B matches exactly apoB₃₃₅₉₋₃₃₆₇. The scopes of claims 2 and 3 thereby become congruent. One of them could hence be deleted without affecting the scope of the claims as a whole, thereby making the set of claim inconcise in the sense of Art.6 PCT.

It is also not clear what the numbering of residues in claim 5 relates to, as it has not been specified where a repeated unit begins or ends; see the use of the word comprising in claims 3 and 4. Claims 1-5 and 13 are considered to be anticipated in the sense of Art.33(2) PCT by D1-D5. Medical use (claim 8) of compounds considered to fall within the scope of these claims is disclosed in each of these documents, and their use in the treatment of viral infection (claims 9 and 10) is known from D1.

Although D1 does not disclose the use of nucleic acids in treatment of viral infection, it is considered to be obvious to the skilled person that if the use of the encoded peptide is disclosed for this purpose, the encoding nucleic acid may also be expressed in the subject to achieve presence of the required protein in the subject. No inventive step in the sense of Art.33(3) PCT can be recognized for such obvious alternatives.

D2-D5 all describe compounds which fall within the general formula of claim 6; see specific indications in the comments to each of the respective citations on the search report. Each of these documents also mentions the use of such compounds as medicaments. Claims 6 and 8 are hence not new in the sense of Art.33(2) PCT.

The specific compounds of claims 7 and 16 are considered to be both new and inventive.

Re: VIII

Claims 10 and 17 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Since many clarity issues of the claims of the present application are intertwined with novelty considerations, they are discussed under item V above. In addition, in claim 16, SEQ.ID.8 is followed by the indication apoB₃₃₅₉₋₃₃₆₇ between brackets. In fact, SEQ.ID.8 represents a direct tandem repeat of apoB₃₃₅₉₋₃₃₆₇. This discrepancy is considered to render this claim unclear in the sense of Art.6 PCT.

As a general observation the ISA considers that novel and inventive subject-matter is clearly present in the underlying application, but that the present claims are much too broad and unclear to be allowable. The description shows clearly that only a very specific group of peptides has antiviral properties, whereas the claims relate to a much broader group of possible compounds, for which the application does not provide support in the sense of Art.5 PCT.